Sulfur Studies. XVIII. Sulfonium Derivatives of p-Phenylphenacyl Bromide[1a]

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The ability of dialkyl sulfides to react with ω-halogenated ketones with the subsequent formation of sulfonium halides has been known for some time. Noteworthy examples of halogenated ketones which have been studied are chloroacetone[2] and ω-bromoacetophenone.[3-5]

In this paper attention has been directed mainly to the use of p-phenylphenacyl bromide as a reagent for alkyl sulfides since the lability of the halogen in p-phenylphenacyl bromide is rather marked. By use of this reagent it was thought that a series of stable sulfonium salts might be obtained whose properties would be suitable for identification purposes. The results, in general, were in accord with this prediction. p-Phenylphenacyl bromide was studied with both simple and mixed alkyl sulfides. The resulting sulfonium bromides were then treated with silver nitrate, sulfate, acetate, benzoate, salicylate, benzenesulfonate, sulfanilate and silver sulfanilamide. In many cases crystalline sulfonium derivatives have been obtained which appear to be very stable. The more stable salts are reported in Tables I and II.

In general, sulfonium salts of strong acids are stable and have good melting points, while those of weak acids are unstable and difficult to isolate. When methanol solutions of the latter type are treated with hydrogen sulfide to remove excess silver ions, a very noteworthy reaction takes place. The reaction results in the formation of p-phenylphenacyl mercaptan as the final product. This compound melts at 109°. An analysis for sulfur gave 13.96%; calculated, 14.03%. It is probable that hydrogen sulfide reacts first with the sulfonium derivative (I) to set free the weak organic acid and forms the unstable sulfhydryl intermediate (II). This latter compound then undergoes fission to give p-phenylphenacyl mercaptan (III) and the dialkyl sulfide (IV). The reaction may be assumed to take place as follows, where X is the acetate, benzoate, salicylate or sulfanilamido radical

$$(C_6H_5C_6H_4COCH_2\overset{\overset{R}{|}}{S}-R')^+X^- + HSH \longrightarrow$$

(I)

$$(C_6H_5C_6H_4COCH_2\overset{\overset{R}{|}}{S}-R')^+SH^- + HX$$

(II)

$$(C_6H_5C_6H_4COCH_2\overset{\overset{R}{|}}{S}-R')^+SH^- \longrightarrow$$

(unstable)

$$C_6H_5C_6H_4COCH_2-SH + R-S-R'$$

(III)   (IV)
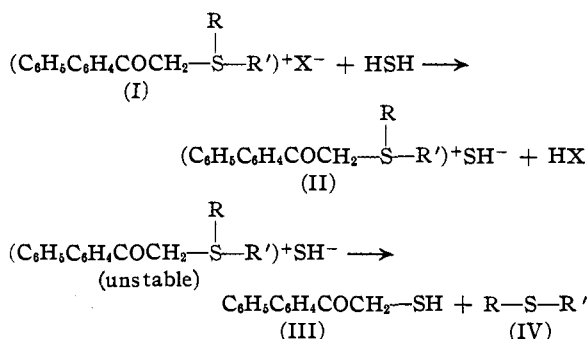
The authors further observed that when methyl n-butyl sulfide is allowed to react with phenacyl bromide in absolute methanol the resulting product is not the anticipated methyl-n-butylphenacylsulfonium bromide, but dimethyl n-butylsulfonium bromide. Molecular decompositions and rearrangements of sulfonium compounds have been observed by other investigators also.[6-8] Ray and Levine[9] have proposed a mechanism whereby such abnormal reactions take place. Such a mechanism seems entirely plausible and serves to explain the anomalous results we have obtained with phenacyl bromide as described above.

Absolute methanol was used as a medium in which to carry out all reactions. A study of the reaction of p-phenylphenacyl bromide with dialkyl sulfides in various solvents confirms an earlier view by Bost and Everett[10] that absolute methanol is best suited for this type of reaction. The solvents investigated in the present work were methanol, ethanol, acetone, acetic anhydride, nitrobenzene, cellosolve, and butyl cellosolve.

Experimental

p-Phenylphenacyl Bromide.—This reagent was obtained from diphenyl by the method of Drake and Bronitsky.[11]

Phenacyl Bromide.—This reagent was prepared by the method of Cowper and Davidson.[12]

Preparation of Sulfonium Compounds: Sulfonium Bromides.—The sulfonium bromides were prepared by dissolving 0.05 mole of dialkyl sulfide in 50 cc. of absolute

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(2) I. G. Farbenind. A.-G., French Patent 807,213.

(3) Smiles, J. Chem. Soc., 77, 1175 (1900).

(4) Balfe, ibid., 2554 (1930).

(5) Stevens, ibid., 69 (1932).

(6) Von Halban, Z. physik. Chem., 67, 129 (1902).

(7) Taylor and Lewis, J. Chem. Soc., 121, 665 (1922).

(8) Gleave, Hughes and Ingold, ibid., 236 (1935).

(9) Ray and Levine, J. Org. Chem., 2, 267 (1937).

(10) Bost and Everett, THIS JOURNAL, 62, 1752 (1940).

(11) Drake and Bronitsky, ibid., 52, 3715 (1930).

(12) Cowper and Davidson, "Org. Syn.," Vol. XIX, 1939, p. 24.

| Alkyl radical | Bromide | | | | | Nitrate | | |
	M. p., °C.	% S Calcd.	% S Found	% Bromine Calcd.	% Bromine Found	M. p., °C.	% S Calcd.	% S Found
Dimethyl	148	9.49	9.42	23.71	24.10	136	10.03	10.19
Diethyl	131	8.77	8.93	21.90	22.43	125	9.22	9.45
Di-n-propyl	117	8.14	8.21	20.38	20.64	118	8.53	8.61
Di-n-butyl	96–107	7.60	7.51	18.96	19.70	138	7.94	8.01
Methyl ethyl	139	9.12	9.11	22.76	23.14	134	9.61	9.52
Methyl n-propyl	131	8.76	8.78	21.89	22.22	121	9.22	9.10
Methyl n-butyl	119	8.44	8.71	21.10	21.13	137	8.86	9.02
Diallyl	72	8.23	8.00					

TABLE II

Data on Dialkyl-p-phenylphenacylsulfonium Bisulfates and Sulfanilates

| Alkyl radical | Bisulfite | | | Sulfanilate | | |
	M. p., °C.	% S Calcd.	% S Found	M. p., °C.	% S Calcd.	% S Found
Dimethyl[a]				166	14.92	15.36
Diethyl	157	16.75	16.78	139	14.02	13.96
Di-n-propyl	152	15.61	15.77	Oil		
Di-n-butyl	172	14.61	14.69	Oil		
Methyl ethyl	155	17.40	17.11	163	14.45	14.77
Methyl n-propyl	Oil			158	14.01	13.83
Methyl n-butyl	168	16.12	16.07	146	13.59	13.58

[a] Forms the normal sulfate, m. p. 148°. *Anal.* for sulfur: calcd., 15.74%; found, 15.85%.

methanol contained in a flask fitted with a reflux condenser. 0.05 mole of p-phenylphenacyl bromide was added and the mixture heated for one to two hours on a steam-bath. The reaction proceeded vigorously and was usually complete in this time. The contents of the flask were cooled and the sulfonium bromide precipitated by the slow addition of absolute ether. The crude salt was then redissolved in methanol and precipitated by ether until a constant melting point of the salt was obtained. Usually two such precipitations were sufficient for this purpose.

Sulfonium Nitrates, Sulfates, Benzenesulfonates and Sulfanilates.—0.05 mole of the sulfonium bromide was dissolved in a minimum quantity of methanol. A slight excess of the calculated amount of powdered silver salt was added and the mixture heated with stirring on a steam-bath. The insoluble silver bromide was removed by filtration and any excess silver ions in the solution were removed by treating the solution with hydrogen sulfide, followed by filtration. The resulting sulfonium salt was then precipitated from the clear methanol solution by the slow addition of absolute ether. These salts can be further purified as given above.

Sulfonium Acetates, Benzoates, Salicylates and Sulfanilamides.—Attempts have been made to prepare these derivatives by using the method given above for the preparation of other sulfonium salts. 0.01 mole of the sulfonium bromide was dissolved in a minimum quantity of methanol and treated with an equivalent amount of powdered silver salt. Silver bromide was filtered from the solution and hydrogen sulfide was then introduced to free the solution of remaining silver ions. In each attempt of this kind a light cream crystalline precipitate was obtained which has since been identified as p-phenylphenacyl mercaptan.

The above crystals of p-phenylphenacyl mercaptan re-

acted positively to alcoholic lead acetate and alcoholic sodium plumbite. It formed a yellow silver mercaptide with silver nitrate and reacted also with sodium hydroxide. A 2,4-dinitrophenylhydrazone was obtained which melted at 159°. Molecular weight determinations using c. p. acetone as a solvent gave values of 237, 229 and 226. The accepted value for p-phenylphenacyl mercaptan is 229. Analyses for sulfur showed a mean value of 13.96%. The accepted value is 14.03%. The compound can be purified by recrystallization from methanol or acetone and melts at 109° without decomposition.

Other Sulfonium Compounds.—Since phenacyl bromide is a common reagent in the organic laboratory, attempts were made to prepare crystalline derivatives of dialkylphenacylsulfonium bromides; however, these met with little success. For example, when appropriate amounts of phenacyl bromide and methyl n-butyl sulfide are allowed to react in absolute methanol dimethyl-n-butylsulfonium bromide is formed rather than the expected dimethylphenacylsulfonium bromide.

Analyses.—The sulfonium bromides were analyzed by direct titration with silver nitrate solution, using the Volhard method. Sulfur was determined by the usual Parr bomb procedure.

In Tables I and II will be found data on the compounds prepared by the above procedures. Di-n-amyl and di-iso-amyl-p-phenylphenacyl sulfonium bromides are oils. Methyl-n-butyl-p-phenylphenacylsulfonium benzenesulfonate melts at 129–134°. Analysis for sulfur gave 14.25%; calculated, 14.09%.

Summary

1. The reaction between p-phenylphenacyl bromide and dialkyl sulfides has been studied in detail.

2. A series of dialkyl-p-phenylphenacylsulfonium bromides, nitrates, sulfates, benzenesulfonates, and sulfanilates have been prepared. The relative stability, solubility and melting points of these salts have been noted.

3. p-Phenylphenacylsulfonium salts of certain organic acids have been found to be unstable when subjected to hydrogen sulfide. These salts decompose to give p-phenylphenacyl mercaptan as a final product. A reaction mechanism is offered to account for the formation of this compound.

4. Methyl-n-butylphenacylsulfonium bromide has been shown to undergo decomposition in the presence of methyl alcohol and dimethyl-n-butylsulfonium bromide has been identified as the final product of this chemical change. An interpretation of the mechanism of this decomposition is noted.

5. Absolute methanol has been found to serve best as a solvent medium for these sulfonium reactions.

6. The dialkyl-p-phenylphenacylsulfonium bromides and nitrates are best suited as derivatives for the sulfides studied.

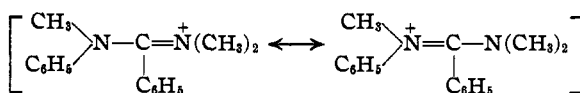# The Tautomeric Character of the Imidazole Ring

BY HARRY GREEN AND ALLAN R. DAY

The active tautomerism of the open chain amidines has long been established. Evidence for this was obtained through the application of three methods, namely, symmetry, fission and substitution tests.[1-3] Confirmatory evidence was supplied by the observation that hydrolytic fission of a single amidine yielded two pairs of products, each pair being derived from one tautomeric form of the parent compound.
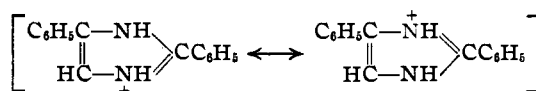
Evidence for the tautomerism of the imidazole ring (a cyclic amidine) was first presented by Kaiser.[4] He obtained only one imidazole from the reduction of 3-nitro-4-acetaminobenzoic acid and 4-nitro-3-acetaminobenzoic acid. Similar evidence was obtained by Gallinek.[5] Fischer and Romer[6] have shown that 2,5(6)-dimethylbenzimidazole reacts tautomerically with methyl iodide, the corresponding 1,2,5- and 1,2,6-trimethylbenzimidazoles being formed in almost equal quantities. Furthermore Fischer and Rigaud,[7] by removing methyl chloride from the hydrochlorides of these products, obtained only one dimethylbenzimidazole.

More recent work by Pyman[3] indicated that the tautomerism of the amidines might not be due to a prototropic change but rather to an electromerization of the cations of their salts. At the time of Pyman's investigations, there was only a single example of the existence of two isomeric forms of an amidine, namely, the occurrence of both 2,4- and 2,5-diphenylimidazole. Pyman

showed that these two compounds were actually isomeric and not polymorphous forms, but they yielded identical salts with any given acid. Further investigation of certain open chain amidines, which contained no potentially mobile hydrogen atom, gave similar results. The isomeric methylphenylaminobenzenylmethylamidine and dimethylaminobenzenylphenylamidine yielded the same methiodide. Pyman recognized the fact that the two quaternary salts possessed the same common cation. His view may be expressed as follows

$$\left[\begin{array}{c} CH_3 \\ C_6H_5 \end{array}\!\!\!\diagdown\!\!N\!-\!C\overset{+}{=}\!N(CH_3)_2 \underset{C_6H_5}{\overset{|}{}} \longleftrightarrow \begin{array}{c} CH_3 \\ C_6H_5 \end{array}\!\!\!\diagdown\!\!\overset{+}{N}\!\!=\!C\!-\!N(CH_3)_2 \underset{C_6H_5}{\overset{|}{}} \right]$$

A similar scheme would apply to the cations of the salts of 2,4- and 2,5-diphenylimidazoles

$$\left[\begin{array}{c} C_6H_5C\!-\!NH \\ \| \\ HC\!-\!NH \\ + \end{array}\!\!\!\diagup\!\!\!\!\diagdown CC_6H_5 \longleftrightarrow \begin{array}{c} C_6H_5C\!-\!\overset{+}{N}H \\ \| \\ HC\!-\!NH \end{array}\!\!\!\diagup\!\!\!\!\diagdown CC_6H_5 \right]$$

More recently, Galimberti[8] has obtained two isomeric naphthimidazoles by treating alcoholic solutions of 1-nitro-β-benznaphthalide and 2-nitro-α-benznaphthalide with zinc and hydrochloric acid. This suggests the possibility that the isolation of the two forms might have been due to the immobilizing influence of the phenyl group and the phenylene group which is attached to the benzene ring of the 2-phenylbenzimidazole structure. When regarded in this light, there is a striking structural similarity between these compounds and the diphenylimidazoles studied by Pyman.

Thus there are really two problems which need to be clarified: (1) can the tautomerism of the

(1) Von Pechmann, *Ber.*, **28**, 1869, 2362 (1895); **30**, 1779 (1897).

(2) Marckwald, *Ann.*, **286**, 343 (1895); Cohen and Marshall, *J. Chem. Soc.*, **97**, 328 (1910).

(3) Pyman, *ibid.*, **123**, 367 (1923).

(4) Kaiser, *Ber.*, **18**, 2942 (1885).

(5) Gallinek, *ibid.*, **30**, 1912 (1897).

(6) Fischer and Romer, *J. prakt. Chem.*, [2] **73**, 424 (1906).

(7) Fischer and Rigaud, *Ber.*, **35**, 1258 (1902).

(8) Galimberti, *Gazz. chim. ital.*, **63**, 96 (1933).